DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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August 19,2014

SIEMENS HEALTHCARE DIAGNOSTICS INC.
ASHA GARTLAND
511 BENEDICT AVE.
TARRYTOWN NY 10591

Re: K141772
Trade/Device Name:
IMMULITE® 2000 Rubella Quantitative IgG Calibration Verification Material
IMMULITE® 2000 *H. pylori* IgG Calibration Verification Material
IMMULITE® 2000 Toxoplasma Quantitative IgG Calibration Verification Material
Regulation Number: 21 CFR 862.1660
Regulation Name: Quality control material (assayed and unassayed)
Regulatory Class: Class I, reserved
Product Code: JJX
Dated: June 30, 2014
Received: July 1, 2014

Dear Ms. Gartland:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Sally A. Hojvat -S

Sally A. Hojvat, Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number: K141772

Device Name:

IMMULITE® 2000 Rubella Quantitative IgG Calibration Verification Material

IMMULITE® 2000 *H. pylori* IgG Calibration Verification Material

IMMULITE® 2000 Toxoplasma Quantitative IgG Calibration Verification Material

Indications for Use:

The IMMULITE® Rubella Quantitative IgG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Rubella Quantitative IgG assay on the IMMULITE 2000 systems.

The IMMULITE® *H. pylori* IgG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE *H. pylori* IgG assay on the IMMULITE 2000 systems.

The IMMULITE® Toxoplasma Quantitative IgG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Toxoplasma Quantitative IgG assay on the IMMULITE 2000 systems.

Prescription Use __X___	And/Or	Over the Counter Use _____
(21 CFR Part 801 Subpart D)		(21 CFR Part 801 Subpart C)

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Section 006: 510(k) Summary

510(k) Summary

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: **k141772**

1. Submitter	
Mailing Address:	Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591
Contact Person:	Asha Gartland Technical Regulatory Affairs Specialist
Phone Number:	(914)-524-3257
Fax Number:	(914)-524-2101
E-mail Address:	asha.gartland@siemens.com
Date Prepared:	June 30, 2014
2. Device Name	
Proprietary Name:	**IMMULITE® 2000 Rubella Quantitative IgG Calibration Verification Material**
Measurand:	Quality Control materials for IMMULITE® 2000 Rubella Quantitative IgG assay
Type of Test:	Calibration Verification Material (CVM) for IMMULITE® 2000 Rubella Quantitative IgG assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Microbiology (83)
3. Predicate Device Name	IMMULITE® 2000 HCG Calibration Verification Material (CVM)
Predicate 510(k) No:	K133128
4. Device Description:	The Calibration Verification Material (CVM) contains one set of four vials each 1.0mL. CVM1 contains negative Rubella IgG in human serum and a buffered bovine protein matrix with preservatives. CVM2, CVM 3 and CVM4 contain various levels of Rubella IgG in human serum and buffered bovine protein matrix with preservatives.

5. Intended Use: **Indication for Use:**	See Indications for Use Statement below: The IMMULITE® Rubella Quantitative IgG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Rubella Quantitative IgG assay on the IMMULITE 2000 systems.
Special Conditions for Use Statement(s):	For prescription use only
Special Instrument Requirements:	IMMULITE® 2000 Systems
6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:	A comparison of the device features, intended use, and other information demonstrates that the IMMULITE® 2000 Rubella Quantitative IgG Calibration Verification Material (CVM) is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: Substantial Equivalence Comparison

SIMILARITIES		
	Candidate Device IMMULITE 2000 Rubella Quantitative IgG CVM	**Predicate Device IMMULITE 2000 HCG CVM**
Intended Use	The IMMULITE® Rubella Quantitative IgG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Rubella Quantitative IgG assay on the IMMULITE 2000 systems.	The IMMULITE® HCG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE HCG assay on the IMMULITE 2000 systems.
Form	Liquid	Same
Storage	≤20°C	Same
Stability	Stable unopened until the expiration date	Same
Levels	4	Same
Use	Single Use Only	Same

	DIFFERENCES	
	Candidate Device IMMULITE 2000 Rubella Quantitative IgG CVM	**Predicate Device IMMULITE 2000 HCG CVM**
Analyte	Rubella IgG	HCG
Matrix	Human serum with Bovine protein and preservatives	Human serum with preservatives

7. Non-Clinical Performance Testing

Performance testing has been carried out to demonstrate that this device meets the performance specifications for its intended use. The following tests were performed on the candidate device.

7.1 Stability Summary:

The stability study was conducted to validate the real-time shelf life and In-Use (Open Component or open vial) claim for the IMMULITE 2000 Rubella Quantitative IgG Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM before and after opening. The IMMULITE® 2000 Rubella Quantitative IgG Calibration Verification Materials are stable up to up to 30 months (2.5 years) when stored at -20°C prior to opening and for 8 hours at ambient or room temperature (15-25°C) after opening.

7.1.1 Stability Protocol Summary:

The CVM study protocols are run as part of the calibrator stability testing. The stability CVMs and reference CVMs are run in duplicate (as a minimum) at the time points shown in **Table 2** and the dose value determined from the reference calibrator curve.

Table 2: Stability Time Points

CVM level	Time-Points (months)			
LRUBCVM1	0	18	24	30
LRUBCVM2	0	18	24	30
LRUBCVM3	0	18	24	30
LRUBCVM4	0	18	24	30

For Open Component testing, the results are determined from 2-point adjustment. Using IMMULITE 2000 Rubella Quantitative IgG kit (L2KRUB) lot 432, CVM lot 090 were tested at 2-hourly intervals for up to 9 hours at ambient or room temperature (15-25°C) conditions.

7.1.2 Stability Acceptance Criteria Summary:

The Acceptance Criteria for the IMMULITE Rubella IgG CVM are in 2 parts. Part 1 consists of guideline acceptance criteria which require dose value of stability calibrator/CVM levels 2 and 3 to fall between ±15% of assigned dose and ±20% of assigned dose for level 4. Part 2 review limits criteria require dose value of the controls to be within 2 Standard Deviation (SD) of the control target value when generated from the stability calibrator curve. If the result is not within acceptable dose range of ±15% for levels 2 and 3 and ±20% for level 4 then additional data review is conducted using part 2 criteria.The acceptance criterion is summarized in **Table 3**.

Table 3 Acceptance criteria for stability of IMMULITE 2000 Rubella Quantitative IgG CVM

CVM level	Assigned Dose (IU/mL)	*Guideline Criteria % difference to assigned dose	Acceptable dose range (IU/mL)	**Review Limits
LRUBCVM1	**0.00**	**Not Applicable**	**≤5.00**	Controls are within 2SD of target on each curve
LRUBCVM2	**9.00**	**±15%**	**7.65 – 10.4**	
LRUBCVM3	**245**	**±15%**	**208 – 282**	
LRUBCVM4	**505**	**±20%**	**404 – 606**	

7.2 Traceability:

The IMMULITE Rubella Quantitative IgG CVMs are traceable to WHO 1st IS RUBI-1-94. The CVMs are manufactured using qualified materials and measurement procedures.

7.3 Value Assignment:

IMMULITE Rubella Quantitative IgG CVMs are 4 level materials which are a subset of 7 level Rubella Quantitative IgG calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of Rubella Quantitative IgG reagents and two point adjustors.

The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The assigned reference calibrators are prepared using Rubella Quantitative IgG antigen stock and are traceable to WHO 1st IS RUBI-1-94. Three levels of commercially available controls and 42 patient serum samples were used to validate calibrator/CVM value assignments.

The CVMs are manufactured using qualified materials and measurement procedures. The IMMULITE Rubella Quantitative IgG calibrators/CVMs were tested on 15 replicates in total, comprised of 5 runs, 3 replicates per run, 4 systems and 3 different reagent kit lots. The CVMs dose values are generated using curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered values for each run on each instrument independently. CVM values are then averaged across all systems. Quality control is performed by calculating the recovery of patient samples and controls using the assigned CVM values. The controls must fall within their target ranges.

7.4 Expected Values/Reference Range:

Each CVM level was tested on 15 replicates in total comprised of 5 runs, 3 replicates per run, 4 systems and 3 different reagent kit lots. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2 Standard Deviation (SD). The expected values are provided in the IMMULITE® 2000 CVM Calibration Verification Material lot-specific package insert.

The expected assay range is 5 to 400 IU/mL. The target values in **Table 4** can be considered as guidelines.

Table 4: Target Values

Analyte target levels	CVM Level	Target Mean (IU/mL)	Standard Deviation (SD)	Guideline ±2SD Range (IU/mL)	
	LRUBCVM1	0.00	-	0.00	≤5.00
	LRUBCVM2	9.15	0.92	7.32	11.0
	LRUBCVM3	195	14.5	166	224
	LRUBCVM4	425	42.5	340	510
Assay Range	5 to 400 IU/mL				

Each laboratory should establish their limits for acceptability based on methodology, clinical significance and medical decision levels of the test analyte. The representative, total precision tabulated in the respective assay instructions for use may be considered as one factor when establishing local, acceptable ranges. The values provided above may be considered as guidelines. Value assignment is lot specific.

Standard/Guidance Documents Referenced**:**

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

Proposed Labeling**:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

8. Conclusion:

The IMMULITE® 2000 Rubella Quantitative IgG Calibration Verification Material is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the FDA cleared IMMULITE® 2000 HCG Calibration Verification Material. The substantial equivalence of the device is supported by the non-clinical testing and was found to be comparable and supports the claims of substantial equivalence, product safety and effectiveness. Based on the testing completed and the comparisons with predicate device, the IMMULITE® 2000 Rubella Quantitative IgG Calibration Verification Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

SIEMENS

510(k) Summary

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: k141772

1. Submitter	
Mailing Address:	Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591
Contact Person:	Asha Gartland Technical Regulatory Affairs Specialist
Phone Number:	(914)-524-3257
Fax Number:	(914)-524-2101
E-mail Address:	asha.gartland@siemens.com
Date Prepared:	June 30th, 2014
2. Device Name	
Proprietary Name:	**IMMULITE® 2000 H. *pylori* IgG Calibration Verification Material**
Measurand:	
Type of Test:	Quality Control material for IMMULITE® 2000 H. *pylori* IgG assay Calibration Verification Material (CVM) for IMMULITE® 2000 H. *pylori* IgG assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Microbiology (83)
3. Predicate Device Name **Predicate 510(k) No:**	IMMULITE® 2000 HCG Calibration Verification Material (CVM) K133128
4. Device Description:	IMMULITE® 2000 H. *pylori* IgG Calibration Verification Material (CVM) contains one 1 mL vial. CVM 1 contains H. *pylori* IgG in human serum and a buffered bovine protein matrix with preservatives.
5. Intended Use: **Indication for Use:**	See Indications for Use Statement below The IMMULITE® H. *pylori* IgG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE H. *pylori* IgG assay on the IMMULITE 2000 systems.

Special Conditions for Use Statement(s): For prescription use only

Special Instrument Requirements: IMMULITE® 2000 Systems

6. Technological Characteristics and Substantial Equivalence Comparison with Predicate: A comparison of the device features, intended use, and other information demonstrates that the IMMULITE® 2000 H. *pylori* IgG Calibration Verification Material (CVM) is substantially equivalent to the predicate device as summarized in **Table 1**.

Table 1: Substantial Equivalence Comparison

SIMILARITIES		
	Candidate Device IMMULITE 2000 H. *pylori* IgG CVM	**Predicate Device IMMULITE 2000 HCG CVM**
Intended Use	The IMMULITE® H. *pylori* IgG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE H. *pylori* IgG assay on the IMMULITE 2000 systems	The IMMULITE® HCG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE HCG assay on the IMMULITE 2000 systems
Form	Liquid	Same
Storage	≤20°C	Same
Stability	Stable unopened until the expiration date	Same
Levels	4	Same
Use	Single Use Only	Same
Form	Liquid	Same

DIFFERENCES		
	Candidate Device IMMULITE 2000 H. *pylori* IgG CVM	**Predicate Device IMMULITE 2000 HCG CVM**
Analyte	H. *pylori* IgG	HCG
Matrix	Human serum with Bovine protein and preservatives	Human serum with preservatives

7. Non-Clinical Performance Testing

Performance testing has been carried out to demonstrate that this device meets the performance specifications for its intended use. The following tests were performed on the candidate device.

7.1 Stability Summary:

The stability study was conducted to validate real-time shelf life and open component (in-use or open vial) for the IMMULITE 2000 *H. pylori* IgG Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM, before and after opening.

The *H. pylori* IgG Calibration Verification Material is stable up to 24 months (2 years) when stored at -20°C prior to opening, and stable for 8 hours at ambient or room temperature (15-25°C) after opening.

7.1.1 Stability Protocol Summary:

The CVM study protocols are run as part of the calibrator stability testing. The stability CVMs and reference CVMs are run in duplicate (as a minimum) at the time points shown in **Table 2** and the dose value determined from the reference calibrator curve.

Table 2: Stability Time Points

CVM Level	Time-Points (months)			
LHPGCVM1	0	12	18	24
LHPGCVM1	0	12	18	24
LHPGCVM1	0	12	18	24
LHPGCVM1	0	12	18	24

For Open Component testing, the results are determined from 2-point adjustment. Using IMMULITE 2000 *H. pylori* IgG (L2KHPG) kit Lot 341, the Lot 090 CVM was tested at 2-hourly intervals for up to 9 hours at ambient or room temperature (15-25°C) conditions.

7.1.2 Stability Acceptance Criteria Summary:

The Acceptance Criteria for the IMMULITE *H. pylori* IgG CVM criteria require the dose value of stability calibrator/CVM to fall within ±10% of the assigned dose.

The acceptance criterion is summarized in **Table 3**.

Table 3 Acceptance criteria for stability of the IMMULITE 2000 *H. pylori* IgG CVM

CVM level	Assigned Dose (U/mL)	Guideline Criteria % difference to assigned dose	Acceptable dose range (U/mL)
LHPGCVM1	**1.07**	**±10%**	**0.96 – 1.18**

7.2 Traceability:
The IMMULITE *H. pylori* IgG CVM is traceable to an internal standard which has been gravimetrically prepared. The CVMs are manufactured using qualified materials and measurement procedures.

7.3 Value Assignment:
H. *pylori* IgG CVM is a single level material; one level of 7 level H. *pylori* IgG calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of H. *pylori* IgG reagents and two point adjustors.

The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The assigned reference calibrators are prepared using H. *pylor*i IgG antigen stock and are traceable to an internal material which has been gravimetrically prepared. Three levels of commercially available controls and 24 patient serum samples were used to validate calibrator/CVM value assignments.

The CVMs are manufactured using qualified materials and measurement procedures. The calibrators/CVMs were tested on 15 replicates in total, comprised of 5 runs, 3 replicates per run, 4 IMMULITE 2000 systems and 3 different reagent kit lots. The CVMs dose values are generated using curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered values for each run on each instrument independently. CVM values are then averaged across all systems. Quality control is performed by calculating the recovery of patient samples, spiked patient samples and controls using the assigned CVM values. The controls must fall within their target ranges.

7.4 Expected Values/Reference Range:
Each CVM level was tested 15 replicates in total, comprised of 5 runs, 3 replicates per run, 4 IMMULITE 2000 systems and 3 different reagent kit lots. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2

Standard Deviation (SD). The expected values are provided in the IMMULITE® 2000 CVM Calibration Verification Material lot-specific package insert. The expected assay range is 0.4 to 8.0 U/mL. The target values in **Table 4** can be considered as guidelines.

Table 4: Target Values

Analyte target levels	CVM Level	Target (U/mL)	Standard Deviation (SD)	Guideline ±2SD Range (U/mL)	
	LHPGCVM1	1.07	0.05425	0.963	1.18
Assay Range	0.4 to 8.0 U/mL				

Each laboratory should establish their limits for acceptability based on methodology, clinical significance and medical decision levels of the test analyte. The representative, total precision tabulated in the respective assay instructions for use may be considered as one factor when establishing local, acceptable ranges. The values provided above may be considered as guidelines. Value assignment is lot specific.

Standard/Guidance Documents Referenced**:**

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

Proposed Labeling**:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

8. Conclusion:

The IMMULITE® 2000 H. *pylori* IgG Calibration Verification Material is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the FDA cleared IMMULITE® 2000 HCG Calibration Verification Material. The substantial equivalence of the device is supported by the non-clinical testing and was found to be comparable and supports the claims of substantial equivalence, product safety and effectiveness. Based on the testing completed and the comparisons with predicate device, the IMMULITE® 2000 H. *pylori* IgG Calibration Verification Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.

SIEMENS

510(k) Summary

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: k141772

1. **Submitter**

Mailing Address:	Siemens Healthcare Diagnostics Inc. 511 Benedict Avenue Tarrytown, NY 10591
Contact Person:	Asha Gartland Technical Regulatory Affairs Specialist
Phone Number:	(914)-524-3257
Fax Number:	(914)-524-2101
E-mail Address:	asha.gartland@siemens.com
Date Prepared:	June 30th, 2014

2. **Device Name**

Proprietary Name:	**IMMULITE® 2000 Toxoplasma Quantitative IgG Calibration Verification Material**
Measurand:	Quality Control materials for IMMULITE® 2000 Toxoplasma Quantitative IgG assay
Type of Test:	Calibration Verification Material (CVM) for IMMULITE® 2000 Toxoplasma Quantitative IgG assay
Regulation Section:	21 CFR 862.1660, Quality Control Material
Classification:	Class I Reserved
Products Code:	JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)
Panel:	Microbiology (83)

3. **Predicate Device Name** IMMULITE® 2000 HCG Calibration Verification Material (CVM) K133128

Predicate 510(k) No:

4. **Device Description:** The Calibration Verification Material (CVM) contains one set of four vials, 1 mL each. CVM1 contains negative Toxoplasma IgG in human serum in a bovine protein/buffer matrix with preservatives. CVM2, CVM3 and CVM4 contain various levels of Toxoplasma IgG in human serum in a bovine protein/buffer matrix with preservatives.

5. Intended Use: **Indication for Use:**	See Indications for Use Statement below The IMMULITE® Toxoplasma Quantitative IgG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Toxoplasma Quantitative IgG assay on the IMMULITE 2000 systems
Special Conditions for Use Statement(s):	For prescription use only
Special Instrument Requirements:	IMMULITE® 2000 Systems
6. Technological Characteristics and Substantial Equivalence Comparison with Predicate:	A comparison of the device features, intended use, and other information demonstrates that the IMMULITE® 2000 Toxoplasma Quantitative IgG Calibration Verification Material (CVM) is substantially equivalent to the predicate device as summarized in **Table 1.**

Table 1: Substantial Equivalence Comparison

SIMILARITIES		
	Candidate Device IMMULITE 2000 Toxoplasma Quantitative IgG CVM	**Predicate Device IMMULITE HCG CVM**
Intended Use	The IMMULITE® Toxoplasma Quantitative IgG CVM Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE Toxoplasma Quantitative IgG assay on the IMMULITE 2000 systems	. The IMMULITE® HCG Calibration Verification Material (CVM) is for in vitro diagnostic use in the verification of calibration of the IMMULITE HCG assay on the IMMULITE 2000 systems.
Form	Liquid	Same
Levels	4	Same
Stability	Stable unopened until the expiration date	Same
Use	Single Use Only	Same
Storage	≤20°C	Same

DIFFERENCES		
	Candidate Device IMMULITE 2000 Toxoplasma Quantitative IgG CVM	**Predicate Device IMMULITE HCG CVM**
Analyte	Toxoplasma Quantitative IgG	HCG
Matrix	Human serum with Bovine protein and preservatives	Human serum with preservatives

7. Non-Clinical Performance Testing

Performance testing has been carried out to demonstrate that this device meets the performance specifications for its intended use. The following tests were performed on the candidate device.

7.1 Stability Summary**:**

The real time stability study was conducted to validate shelf life claim and In-Use (Open Component or open vial) claim for the IMMULITE 2000 Toxoplasma Quantitative IgG Calibration Verification Material (CVM) to ensure that it maintains optimal product performance on IMMULITE 2000 platforms throughout the established shelf life of the CVM before and after opening.The IMMULITE® 2000 Toxoplasma Quantitative IgG Calibration

Verification Materials (CVMs) are up 3 years when stored at -20°C prior to opening and stable for 8 hours at ambient or room temperature (15-25°C) after opening.

7.1.1 Stability Protocol Summary:

The CVM study protocols are run as part of the calibrator stability testing. The stability CVMs and reference CVMs are run in duplicate (as a minimum) at the time points shown in **Table 2** and the dose value determined from the reference calibrator curve.

Table 2: Stability Time Points

CVM Level	Time-Points (Months)			
LTXPCVM1	0	24	30	36
LTXPCVM2	0	24	30	36
LTXPCVM3	0	24	30	36
LTXPCVM4	0	24	30	36

For Open Component testing, the results are determined from 2-point adjustment. Using L2KTXP Kit Lot 394, Lot 090 CVMs were tested at 2-hourly intervals for up to 9 hours at ambient or room temperature (15-25°C) conditions.

7.1.2 Stability Acceptance Criteria Summary:

The Acceptance Criteria for the IMMULITE 2000 Toxoplasma Quantitative IgG CVM are in 2 parts. Part 1 consists of guideline acceptance criteria which require dose value of stability calibrator/CVM levels 2 and 3 to fall between ±10% of assigned dose and ±24% for level 4. Part 2 review limits criteria require dose value of the controls to be within 2 Standard Deviations (SD) of the control target value when generated from the stability calibrator curve. If the result is not within acceptable dose range of ±10% for levels 2 and 3 and ±24% for level 4 then additional data review is conducted using part 2 criteria.

The acceptance criterion is summarized in **Table 3.**

Table 3: Acceptance criteria for stability of IMMULITE 2000 Toxoplasma Quantitative IgG CVM

CVM level	Assigned Dose (IU/mL)	*Guideline Criteria % difference to assigned dose	Acceptable dose range (pg/mL) (IU/mL)	Review Limits
LTXPCVM1	0.00	Not Applicable	≤5.00	Controls are within 2SD of target on each curve
LTXPCVM2	10.6	±10%	9.5 – 11.7	
LTXPCVM3	73.5	±10%	66.2 – 80.9	
LTXPCVM4	370	±24%	281 – 459	

7.2 Traceability:
The IMMULITE Toxoplasma Quantitative IgG calibrators and therefore CVMs are value assigned using assigned reference calibrators and are traceable to WHO 3rd IS for Anti-Toxoplasma Serum, Human. The calibrators/CVMs are manufactured using qualified materials and measurement procedures.

7.3 Value Assignment:
IMMULITE Toxoplasma Quantitative IgG CVMs are 4 level materials which are a subset of 6 level Toxoplasma Quantitative IgG calibrators. Calibrators are not commercialized but are used internally during manufacture and release testing of Toxoplasma Quantitative IgG reagents and two point adjustors. The IMMULITE calibrators and therefore CVMs are value assigned using assigned reference calibrators. The assigned reference calibrators are prepared using human serum with IgG positive to Toxoplasma and human serum with IgG negative to Toxoplasma which are combined and spiked in the buffered bovine protein matrix. Three levels of commercially available controls and 63 serum samples (40 patient samples and 23 normal samples) were used to validate calibrator/CVM value assignments.

The CVMs are manufactured using qualified materials and measurement procedures. The CVMs were tested on 15 replicates in total, comprised of 5 runs, 3 replicates per run, 5 IMMULITE 2000 systems and 3 different reagent kit lots. The CVMs dose values are generated using curve generated by assigned reference calibrators. The CVM values are calculated based on the recovered values for each run on each instrument independently. CVM values are then averaged across all systems. Quality control is performed by calculating the recovery of patient samples, spiked patient samples and controls using the assigned CVM values. The controls must fall within their target ranges.

7.4 Expected Values/Reference Range:
Each CVM level was tested on 15 replicates in total comprised of 5 runs, 3 replicates per run, 5 IMMULITE 2000 systems and 3 different reagent kit lots. The Guideline Range (95% confidence interval) for each CVM level was established based on the Target Mean and ± 2 Standard Deviation (SD). The expected values are provided in the IMMULITE® 2000 Toxoplasma Quantitative IgG CVM Calibration Verification Material lot-specific package insert. The expected assay range is 5 to 250 IU/mL. The target values in **Table 4** can be considered as guidelines.

Table 4: Target Values

Analyte target levels	CVM Level	Target Mean (IU/mL)	Standard Deviation (SD)	Guideline ±2SD Range (IU/mL)	
	LTXPCVM1	0.00	-	0.00	≤5.00
	LTXPCVM2	10.1	0.7525	8.59	11.6
	LTXPCVM3	73.5	5.5	62.5	84.5
	LTXPCVM4	272	32.5	207	337
Assay Range	5 to 250 IU/mL				

Each laboratory should establish their limits for acceptability based on methodology, clinical significance and medical decision levels of the test analyte. The representative, total precision tabulated in the respective assay instructions for use may be considered as one factor when establishing local, acceptable ranges. The values provided above may be considered as guidelines. Value assignment is lot specific.

Standard/Guidance Documents Referenced**:**

- CEN 13640 Stability Testing of In Vitro Diagnostic Reagents
- Guidance for Industry – Abbreviated 510(k) Submissions for In Vitro Diagnostic Calibrators
- Guidance for Industry and FDA Staff – Assayed and Unassayed Quality Control Material

Proposed Labeling**:**
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

8. Conclusion:

The IMMULITE® 2000 Toxoplasma Quantitative IgG Calibration Verification Material is substantially equivalent to other products in commercial distribution intended for similar use. Most notably, it is substantially equivalent to the FDA cleared IMMULITE® 2000 HCG Calibration Verification Material The substantial equivalence of the device is supported by the non-clinical testing and was found to be comparable and supports the claims of substantial equivalence, product safety and effectiveness. Based on the testing completed and the comparisons with predicate device, the IMMULITE® 2000 Toxoplasma Quantitative IgG Calibration Verification Material does not raise any new questions on safety and effectiveness and the results support a determination of substantial equivalence.